### ETONOGESTREL/ETHINYL ESTRADIOL

**Generic (Trade Name):** Etonogestrel/ethinyl estradiol (NuvaRing®)

**Manufacturer:** Organon Inc.

**Indication:** Contraceptive ring

**Current Regulatory Status:** Organon gained FDA approval for marketing in the U.S. in late 2001. The current plan is to market this product in the U.S. in mid-2002, after appropriate manufacturing facilities have been put in place to meet the anticipated demand. A submission has been made to Health Canada for approval, however the company does not wish to speculate about a possible availability date.

**Description:** NuvaRing® is a device consisting of ethylene vinylacetate copolymers which releases 0.12 mg of etonogesterel and 0.015 mg of ethinyl estradiol per day into the vagina for 21 consecutive days. The wearer then observes a seven day "ring-free" period, after which a new ring is inserted. The product comes in sachets, and is supplied as one or three in a box. The rings are to be stored at room temperature. If exposed to room temperature, the expiry date is shortened to four months. Users are still at risk for contracting sexually transmitted diseases, similar to IUDs or the oral contraceptive pill.

**Current Treatment:** Options for contraceptive methods are vast. Natural methods can be used, such as abstinence, withdrawal, or rhythm methods. Barrier methods can be successful and include condoms, foam with spermacides and diaphragms. Pharmacologics are another opportunity including implants, IUDs, and the most popular agents, oral contraceptives. For those looking for more permanency, sterilization of the male or female can be surgically achieved. Certainly the reliability of these methods vary greatly, based on the diligence of the user and plain luck.

**Cost:** This product has not yet been launched globally, therefore information on pricing at this time is unavailable.

**Evidence:** There are two large trials including over 2,500 women in total. The largest conducted by Roumen et al, was a one-year, open-label, non-comparative multicentre study carried out in numerous countries in Europe. Based on pregnancy results after one year of use, the Pearl Index was 0.65 (95% CI 0.24-1.14). Tolerability was quite good, with the most frequently reported adverse events including vaginitis, headache and leukorrhoea. Approximately 30 percent of the intent-to-treat population discontinued therapy prematurely, mostly due to adverse events. Most women who completed the trial indicated that the placement and removal of the ring was easy. Eighty seven and 74 percent of users and partners, respectively, suggested that they did not feel the ring.
Etonogestrel/ethinyl estradiol during intercourse. Looking at the data accumulated to date, it is reported that during 13 cycles of ring use (i.e. one year), one or two patients in 100 became pregnant. Mulders and Dieben suggest that ovarian suppression achieved with this device was comparable to a desogesterel 150 mcg/ethinyl estradiol 30 mcg combined oral contraceptive (i.e. Marvelon®).

Commentary:
The ring was developed as an effective means of contraception, while using lower doses which may minimize the side effects attributed to oral formulations. As non-oral routes may afford higher bioavailability, this underscores why this route of administration has been explored. Some patients may find this method appealing, as it is only administered once monthly, and by all accounts, seems fairly simple to use. However, it still has the same contraindications as other hormonal agents, and some patients may not feel comfortable with its intimacy of application or the thought of possible perception of this agent by themselves or their partner.

References:


